

CLAIMS

We claim:

1. A multilayer microculture comprising a plurality of three-dimensional non-fluid layers, wherein each layer comprises at least one cell type and a biopolymer selected from the group consisting of collagen, chitosan, fibronectin, matrigel, fibrin, and mixtures thereof, and wherein each layer comprises a width less than one millimeter.
2. The microculture according to claim 1 wherein each layer comprises a distinct cell type.
3. The microculture according to claim 1 wherein at least one layer comprises a plurality of cell types.
4. The microculture according to claim 1 wherein at least one layer is attached to an optically transparent support.
5. The microculture according to claim 1 wherein said layers comprises a first layer that is immobilized and wherein said first layer is resistant to a shear force associated with a 5 μ l/min lateral flow of a cell-biopolymer fluid across the face of said first layer.
6. The microculture according to claim 1 wherein said microculture mimics a mammalian tissue.
7. The microculture according to claim 1 wherein said cell type is a non-contractile cell.
8. A method for producing a multilayer microculture comprising:
 - (a) introducing a first material comprising a first cell matrix compound and a first cell type to a microstructure by microfluidic delivery, wherein said material is introduced as a fluid;
 - (b) attaching said first material to at least one surface of said microstructure;
 - (c) incubating said first material under conditions suitable for at least one component of said material to polymerize and for said material to contract in at least one dimension; and

(d) repeating step (a) with a second material comprising a second cell matrix compound and a second cell type;

(e) attaching said second material to said first material; and

(f) incubating said second material under conditions suitable for at least one component of said second material to polymerize, thereby producing a multilayer microculture.

9. The method according to claim 8 wherein said first cell type and said second cell type are the same.

10. The method according to claim 8 further comprising:

(a) incubating said second material under conditions suitable for said second material to contract; and

(b) preparing a third layer of microculture by repeating steps (d)-(f) of claim 8.

11. The method according to claim 8 wherein said microstructure comprises a plurality of microchannels and at least one microfluidic aperture.

12. The method according to claim 8 wherein said material is a cell culture medium.

13. The method according to claim 8 wherein said conditions comprise time sufficient for said material to become a gel.

14. The method according to claim 8 further comprising attaching said material to said support.

15. The method according to claim 14 wherein said support is a derivatized glass.

16. The method according to claim 15 wherein said glass is derivatized by the presence of amine groups.

17. The method according to claim 16 further comprising an aldehyde cross-linker attached to at least one of said amino groups.

18. A method of screening for a biohazardous material comprising:

(a) incorporating a test material into at least one layer of a microculture according to claim 1;

(b) incubating said microculture; and

(c) measuring culture development in the presence of said test material relative to the culture development in the absence of said test material, wherein a difference in response relative to a microculture lacking said test material identifies a biohazardous material.

19. A method for monitoring physiological health comprising:

(a) obtaining a biological sample from a mammalian subject;

(b) incorporating the biological sample into at least one layer of a microculture according to claim 1;

(c) incubating said microculture; and

(d) measuring culture development in the presence of said biological sample relative to the culture development in the absence of said biological sample, wherein a difference in response relative to a microculture lacking said biological sample provides an indication of the physiological health of said subject.

20. A method for identifying a modulator of tissue development comprising:

(a) incorporating a candidate modulator of tissue development into at least one layer of a microculture according to claim 1;

(b) incubating said microculture; and

(c) measuring the tissue development in the presence of said candidate modulator relative to the tissue development in the absence of said candidate modulator, wherein a difference in response relative to a microculture lacking said candidate modulator identifies a modulator of tissue development.

21. A method for identifying a modulator of cell-cell interaction comprising:

(a) incorporating a candidate modulator of cell-cell interaction into at least one layer of a microculture according to claim 1;

(b) incubating said microculture; and

(c) measuring cell-cell interaction in the presence of said candidate modulator relative to cell-cell interaction in the absence of said candidate modulator, wherein a difference in response relative to a microculture lacking said candidate modulator identifies a modulator of cell-cell interaction.

22. A method for identifying a modulator of cell migration comprising:

(a) incorporating a candidate modulator of cell migration into at least one layer of a microculture according to claim 1;

(b) incubating said microculture; and

(c) measuring cell migration in the presence of said candidate modulator relative to cell migration in the absence of said candidate modulator, wherein a difference in response relative to a microculture lacking said candidate modulator identifies a modulator of cell migration.

23. A method for identifying a modulator of cell proliferation comprising:

(a) incorporating a candidate modulator of cell proliferation into at least one layer of a microculture according to claim 1;

(b) incubating said microculture; and

(c) measuring cell proliferation in the presence of said candidate modulator relative to cell proliferation in the absence of said candidate modulator, wherein a difference in response relative to a microculture lacking said candidate modulator identifies a modulator of cell proliferation.

24. A method for identifying a modulator of cell adhesion comprising:

(a) incorporating a candidate modulator of cell adhesion into at least one layer of a microculture according to claim 1;

(b) incubating said microculture; and

(c) measuring cell adhesion in the presence of said candidate modulator relative to cell adhesion in the absence of said candidate modulator, wherein a difference in response relative to a microculture lacking said candidate modulator identifies a modulator of cell adhesion.

25. A kit for performing the method according to any one of claims 15-21, comprising a multilayer microculture comprising a plurality of three-dimensional non-fluid layers, wherein each layer comprises at least one cell type and a biopolymer selected from the group consisting of collagen, chitosan, fibronectin, matrigel, fibrin, and mixtures thereof, and wherein each layer comprises a width less than one millimeter, and package instructions for using the contents of said kit to perform said method.